BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

FIG. 1A

GAATTCTCTGGACTGAGGCTCCAGTTCTGGCCTTTGGGG

TTCAAGATCACTGGGACCAGGCCGTGATCTCTATGCCCGAGTCTCAACCCTCAACTGTC

ACCCCAAGGCACTTGGGACGTCCTGGACAGACCGAGTCCCGGGAAGCCCCAGCACTGCC

***

GCTGCCACACTGCCCTGAGCCCAAATGGGGGAGTGAGAGGCCA TAG CTG TCT GGC

S1 S5 S10 S15
Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu
ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC
216 225 234 243 252

S20 S25 S29 1
Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu
CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA CTG
261 270 279 288 297

5 10 15
Val Pro His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro
GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA GAT AGT GTG TGT CCC
306 315 324 333 342

20 25 30
Gln Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr
CAA GGA AAA TAT ATC CAC CCT CAA AAT AAT TCG ATT TGC TGT ACC
351 360 369 378 387

35 40 45
Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro
AAG TGC CAC AAA GGA ACC TAC TTG TAC AAT GAC TGT CCA GGC CCG
396 405 414 423 432

50 55 60
Gly Gln Asp Thr Asp Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr
GGG CAG GAT ACG GAC TGC AGG GAG TGT GAG AGC GGC TCC TTC ACC
441 450 459 468 477

65 70 75
Ala Ser Glu Asn His Leu Arg His Cys Leu Ser Cys Ser Lys Cys
GCT TCA GAA AAC CAC CTC AGA CAC TGC CTC AGC TGC TCC AAA TGC
486 495 504 513 522

80 85 90
Arg Lys Glu Met Gly Gln Val Glu Ile Ser Ser Cys Thr Val Asp
CGA AAG GAA ATG GGT CAG GTG GAG ATC TCT TCT TGC ACA GTG GAC
531 540 549 558 567

FIG. 1B

```
                95                  100                 105
Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr
CGG GAC ACC GTG TGT GGC TGC AGG AAG AAC CAG TAC CGG CAT TAT
  576         585         594         603         612

            110                 115                 120
Trp Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu
TGG AGT GAA AAC CTT TTC CAG TGC TTC AAT TGC AGC CTC TGC CTC
  621         630         639         648         657

            125                 130                 135
Asn Gly Thr Val His Leu Ser Cys Gln Glu Lys Gln Asn Thr Val
AAT GGG ACC GTG CAC CTC TCC TGC CAG GAG AAA CAG AAC ACC GTG
  666         675         684         693         702

            140                 145                 150
Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu Asn Glu Cys Val
TGC ACC TGC CAT GCA GGT TTC TTT CTA AGA GAA AAC GAG TGT GTC
  711         720         729         738         747

            155                 160                 165
Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr Lys Leu Cys
TCC TGT AGT AAC TGT AAG AAA AGC CTG GAG TGC ACG AAG TTG TGC
  756         765         774         783         792

            170                 175                 180
Leu Pro Gln Ile Glu Asn Val Lys Gly Thr Glu Asp Ser Gly Thr
CTA CCC CAG ATT GAG AAT GTT AAG GGC ACT GAG GAC TCA GGC ACC
  801         810         819         828         837

            185                 190                 195
Thr Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu Leu
ACA GTG CTG TTG CCC CTG GTC ATT TTC TTT GGT CTT TGC CTT TTA
  846         855         864         873         882

            200                 205                 210
Ser Leu Leu Phe Ile Gly Leu Met Tyr Arg Tyr Gln Arg Trp Lys
TCC CTC CTC TTC ATT GGT TTA ATG TAT CGC TAC CAA CGG TGG AAG
  891         900         909         918         927

            215                 220                 225
Ser Lys Leu Tyr Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys
TCC AAG CTC TAC TCC ATT GTT TGT GGG AAA TCG ACA CCT GAA AAA
  936         945         954         963         972

            230                 235                 240
Glu Gly Glu Leu Glu Gly Thr Thr Thr Lys Pro Leu Ala Pro Asn
GAG GGG GAG CTT GAA GGA ACT ACT ACT AAG CCC CTG GCC CCA AAC
  981         990         999        1008        1017
```

FIG. 1C

```
                245                 250                 255
Pro Ser Phe Ser Pro Thr Pro Gly Phe Thr Pro Thr Leu Gly Phe
CCA AGC TTC AGT CCC ACT CCA GGC TTC ACC CCC ACC CTG GGC TTC
 1026        1035        1044        1053        1062

                260                 265                 270
Ser Pro Val Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr Tyr Thr
AGT CCC GTG CCC AGT TCC ACC TTC ACC TCC AGC TCC ACC TAT ACC
 1071        1080        1089        1098        1107

                275                 280                 285
Pro Gly Asp Cys Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala
CCC GGT GAC TGT CCC AAC TTT GCG GCT CCC CGC AGA GAG GTG GCA
 1116        1125        1134        1143        1152

                290                 295                 300
Pro Pro Tyr Gln Gly Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala
CCA CCC TAT CAG GGG GCT GAC CCC ATC CTT GCG ACA GCC CTC GCC
 1161        1170        1179        1188        1197

                305                 310                 315
Ser Asp Pro Ile Pro Asn Pro Leu Gln Lys Trp Glu Asp Ser Ala
TCC GAC CCC ATC CCC AAC CCC CTT CAG AAG TGG GAG GAC AGC GCC
 1206        1215        1224        1233        1242

                320                 325                 330
His Lys Pro Gln Ser Leu Asp Thr Asp Asp Pro Ala Thr Leu Tyr
CAC AAG CCA CAG AGC CTA GAC ACT GAT GAC CCC GCG ACG CTG TAC
 1251        1260        1269        1278        1287

                335                 340
Ala Val Val Glu Asn Val Pro Pro Leu Arg Trp
GCC GTG GTG GAG AAC GTG CCC CCG TTG CGC TGG AA GGAATTC
 1296        1305        1314        1323        1332
```

FIG. 2

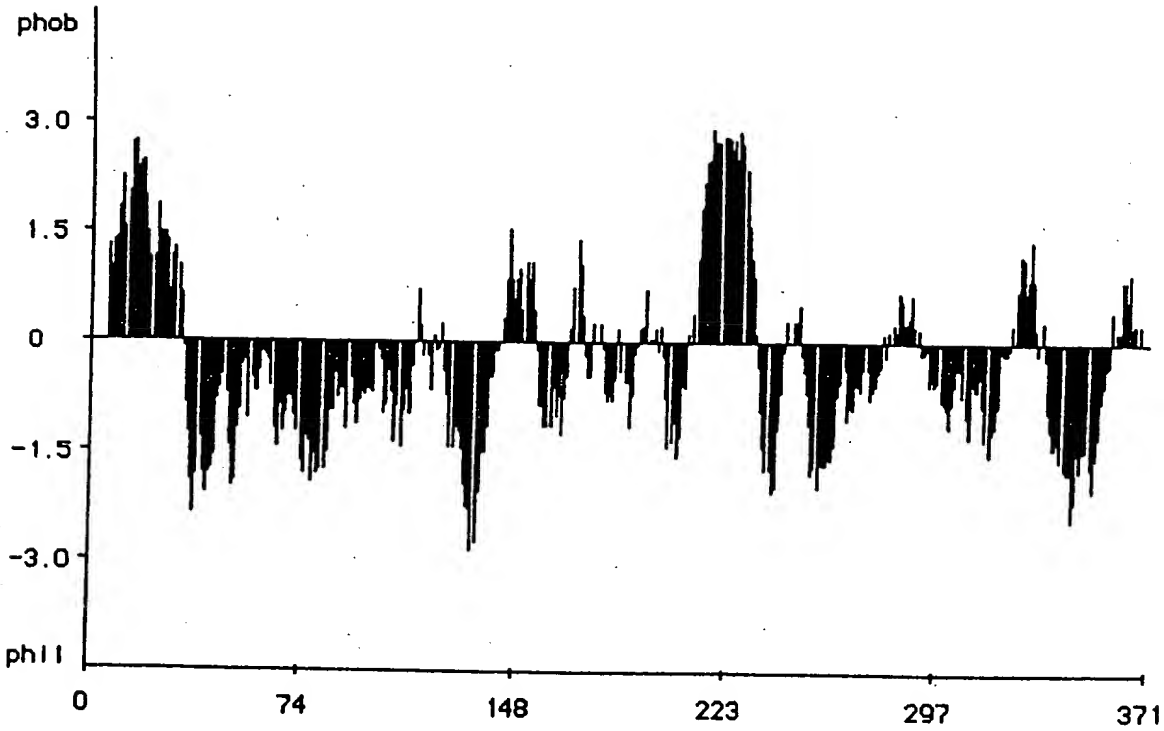


FIG. 3A

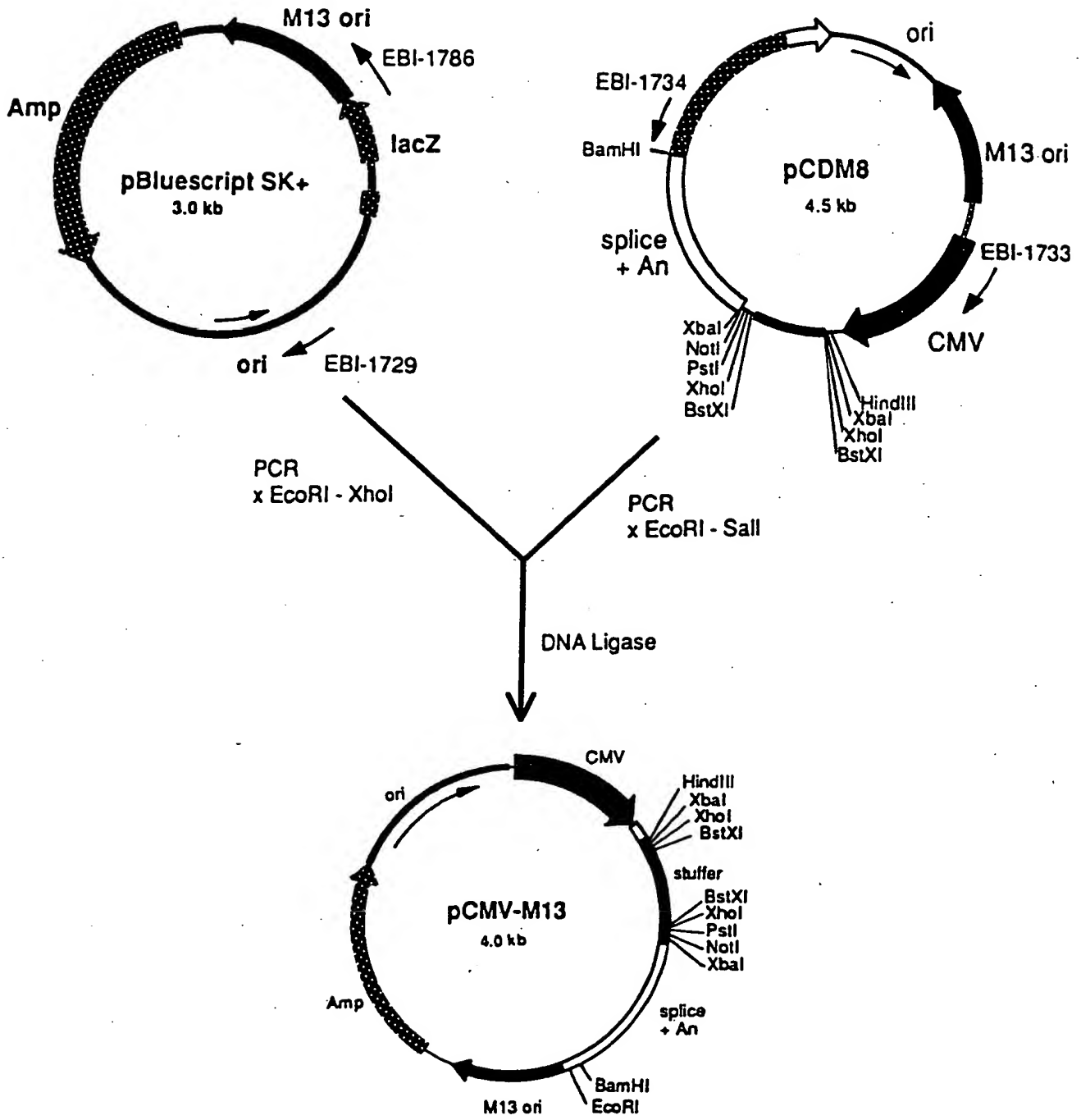

M13 ori
EBI-1786
Amp
lacZ
pBluescript SK+
3.0 kb
ori
EBI-1729
ori
EBI-1734
BamHI
pCDM8
4.5 kb
M13 ori
splice
+ An
EBI-1733
CMV
XbaI
NotI
PstI
XhoI
BstXI
HindIII
XbaI
XhoI
BstXI
PCR
x EcoRI - XhoI
PCR
x EcoRI - SalI
DNA Ligase
CMV
ori
HindIII
XbaI
XhoI
BstXI
stuffer
pCMV-M13
4.0 kb
BstXI
XhoI
PstI
NotI
XbaI
Amp
splice
+ An
BamHI
EcoRI
M13 ori

FIG. 3B

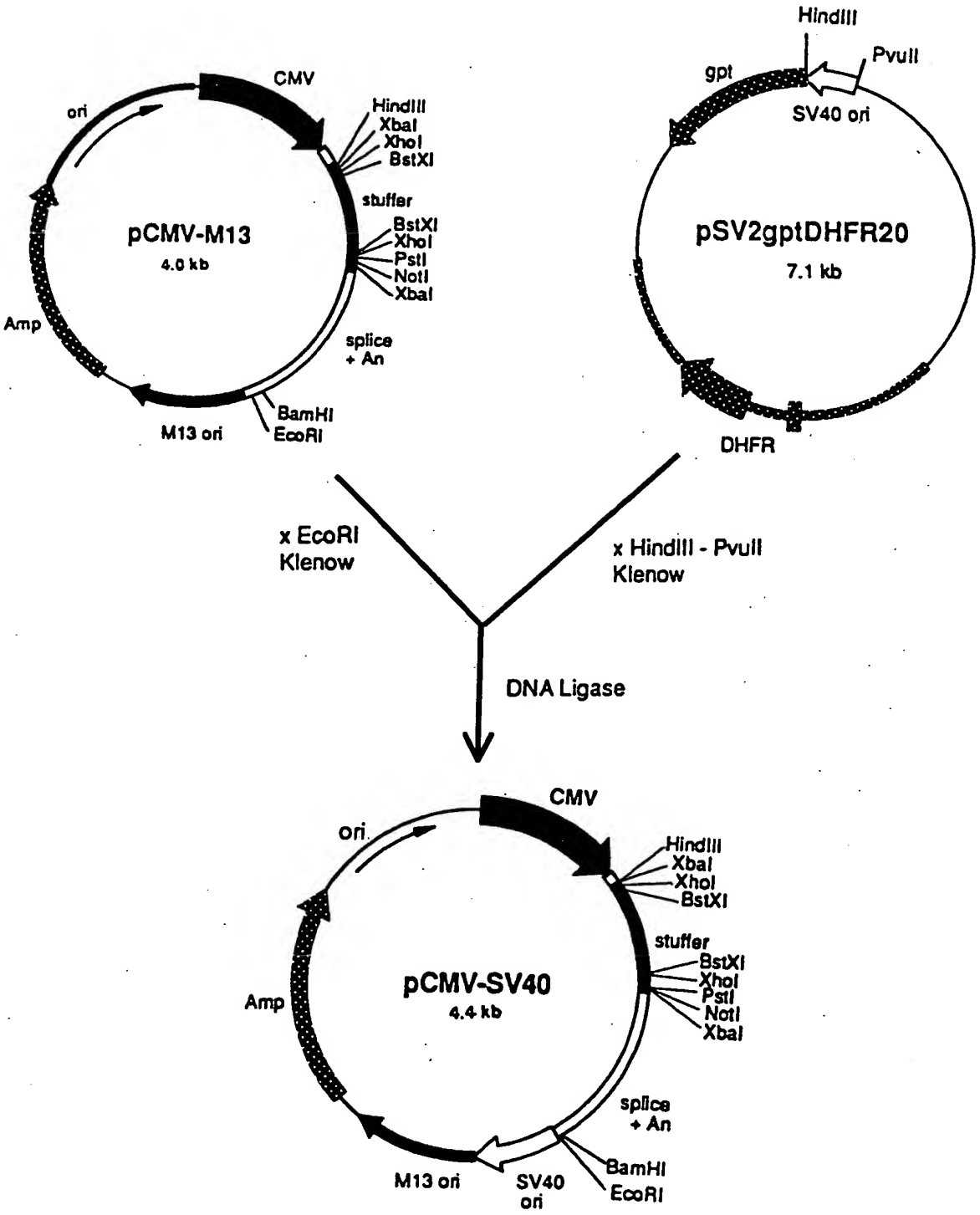

pCMV-M13
4.0 kb
CMV
ori
HindIII
XbaI
XhoI
BstXI
stuffer
BstXI
XhoI
PstI
NotI
XbaI
splice
+ An
BamHI
EcoRI
M13 ori
Amp
pSV2gptDHFR20
7.1 kb
HindIII
PvuII
gpt
SV40 ori
DHFR
x EcoRI
Klenow
x HindIII - PvuII
Klenow
DNA Ligase
pCMV-SV40
4.4 kb
CMV
ori
HindIII
XbaI
XhoI
BstXI
stuffer
BstXI
XhoI
PstI
NotI
XbaI
splice
+ An
BamHI
EcoRI
M13 ori
SV40
ori
Amp

FIG. 4A

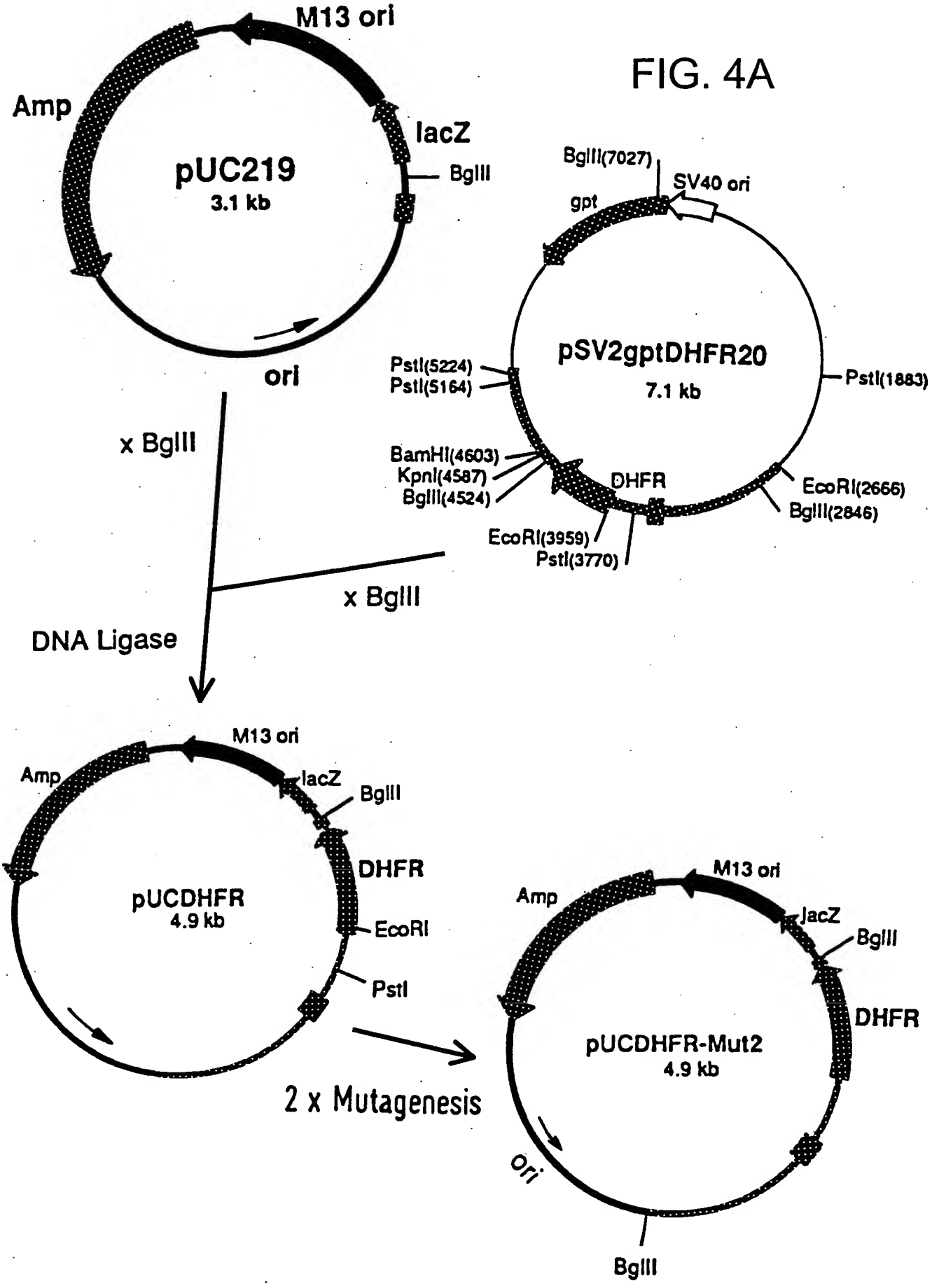
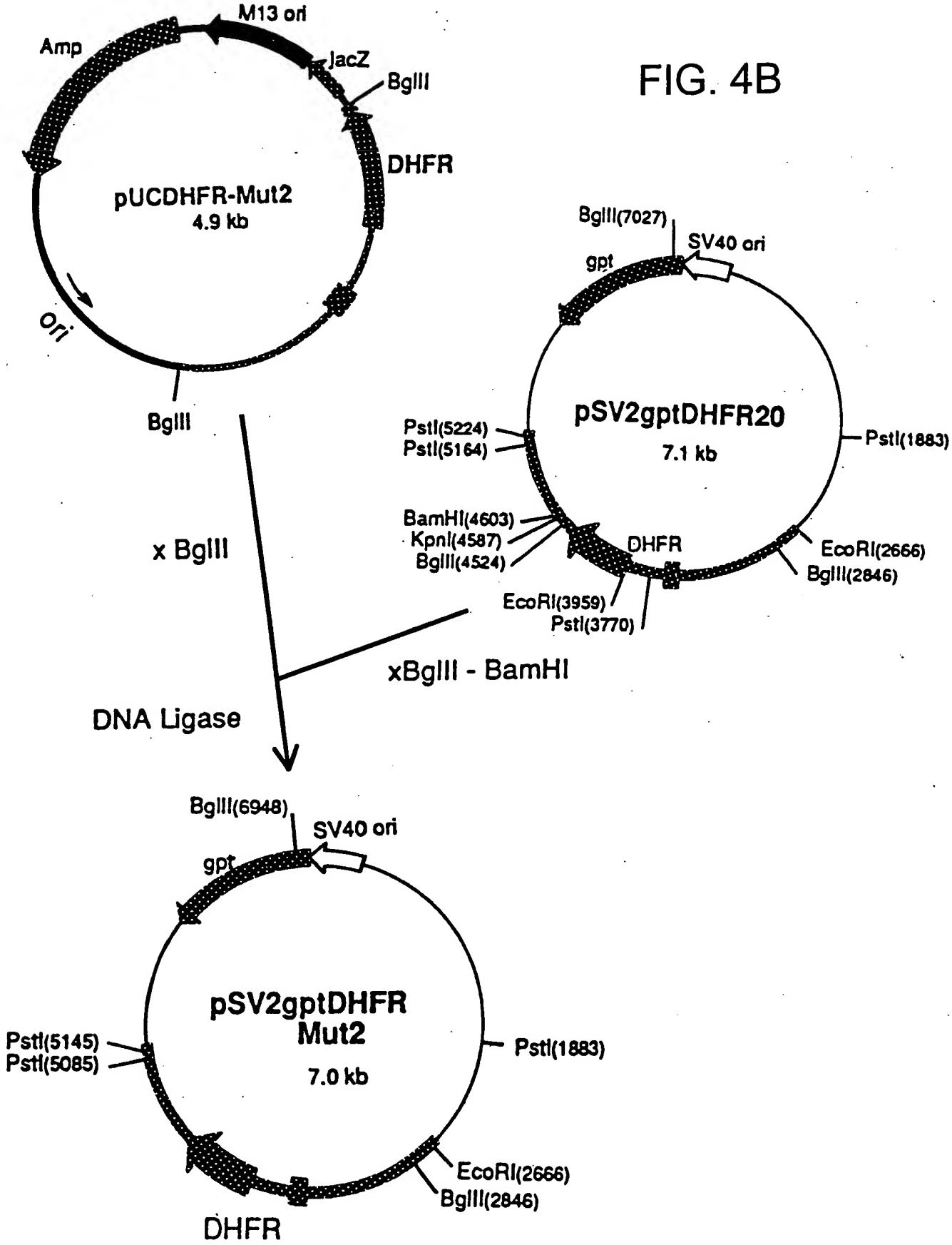

M13 ori
Amp
lacZ
pUC219
3.1 kb
BglII
ori
x BglII
BglII(7027)
SV40 ori
gpt
pSV2gptDHFR20
7.1 kb
PstI(5224)
PstI(5164)
PstI(1883)
BamHI(4603)
KpnI(4587)
BglII(4524)
DHFR
EcoRI(2666)
BglII(2846)
EcoRI(3959)
PstI(3770)
x BglII
DNA Ligase
M13 ori
Amp
lacZ
BglII
DHFR
pUCDHFR
4.9 kb
EcoRI
PstI
2 x Mutagenesis
M13 ori
Amp
lacZ
BglII
DHFR
pUCDHFR-Mut2
4.9 kb
ori
BglII

FIG. 4B


M13 ori
Amp
lacZ
BglII
DHFR
pUCDHFR-Mut2
4.9 kb
ori
BglII
x BglII
BglII(7027)
SV40 ori
gpt
pSV2gptDHFR20
7.1 kb
PstI(5224)
PstI(5164)
PstI(1883)
BamHI(4603)
KpnI(4587)
BglII(4524)
DHFR
EcoRI(2666)
BglII(2846)
EcoRI(3959)
PstI(3770)
xBglII - BamHI
DNA Ligase
BglII(6948)
SV40 ori
gpt
pSV2gptDHFR
Mut2
7.0 kb
PstI(5145)
PstI(5085)
PstI(1883)
EcoRI(2666)
BglII(2846)
DHFR

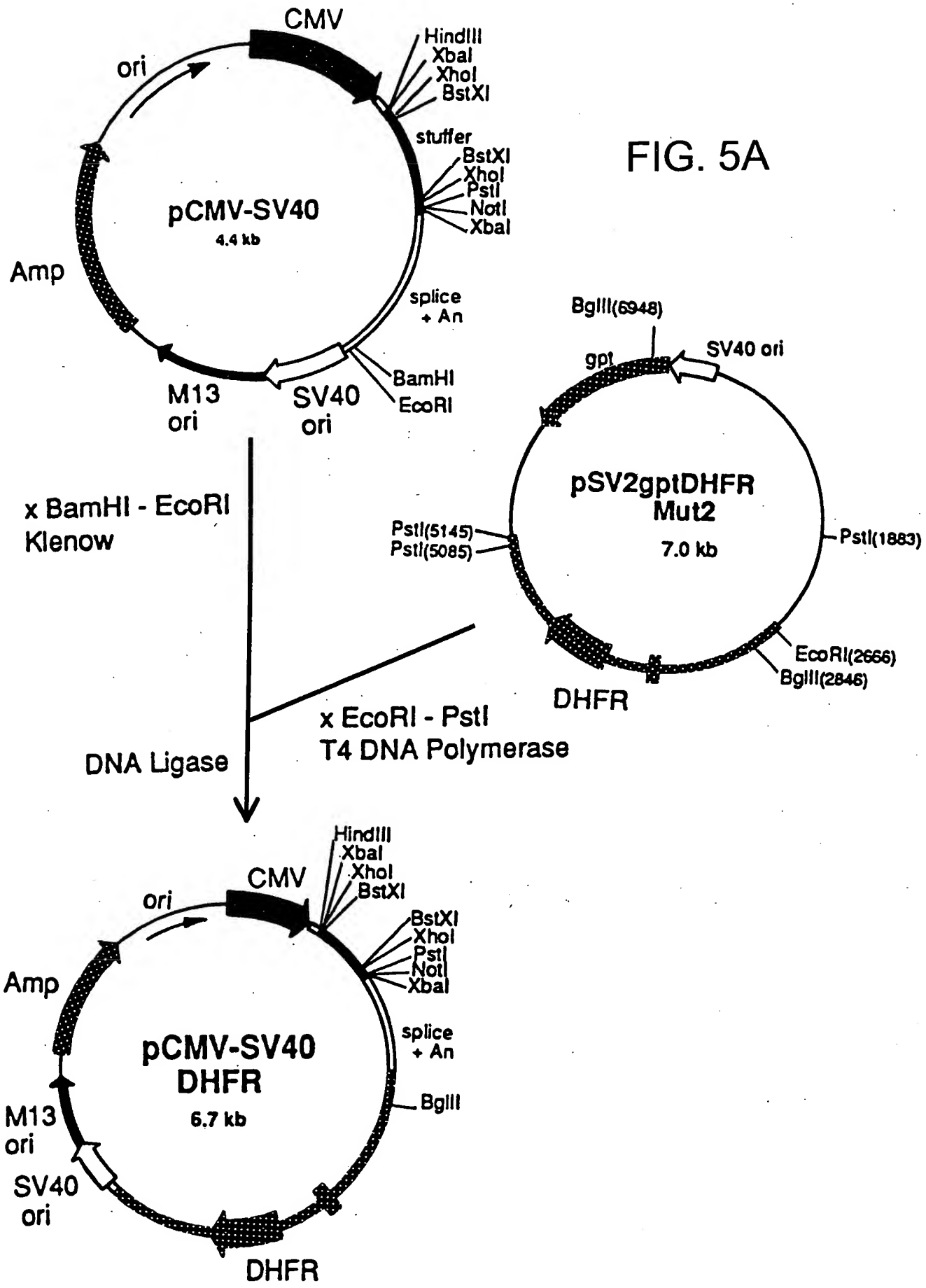

CMV
HindIII
XbaI
XhoI
BstXI
ori
stuffer
BstXI
XhoI
PstI
NotI
XbaI
pCMV-SV40
4.4 kb
Amp
splice
+ An
BamHI
EcoRI
M13
ori
SV40
ori
x BamHI - EcoRI
Klenow
BglII(6948)
gpt
SV40 ori
pSV2gptDHFR
Mut2
7.0 kb
PstI(5145)
PstI(5085)
PstI(1883)
EcoRI(2666)
BglII(2846)
DHFR
x EcoRI - PstI
T4 DNA Polymerase
DNA Ligase
HindIII
XbaI
XhoI
BstXI
CMV
ori
BstXI
XhoI
PstI
NotI
XbaI
Amp
pCMV-SV40
DHFR
6.7 kb
splice
+ An
BglII
M13
ori
SV40
ori
DHFR

FIG. 5A

FIG. 5B

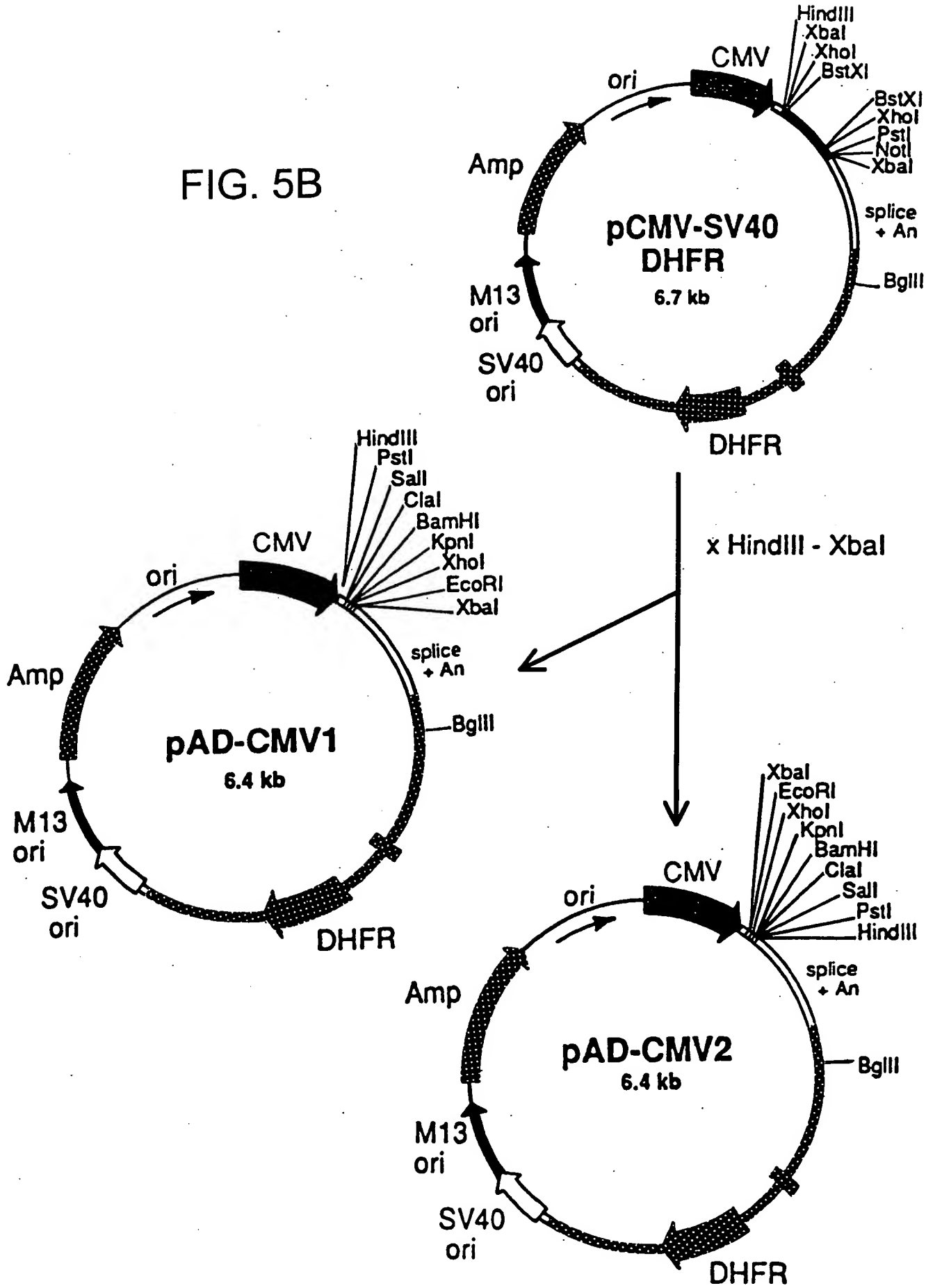

HindIII
XbaI
XhoI
BstXI
CMV
ori
BstXI
XhoI
PstI
NotI
XbaI
Amp
splice
+ An
pCMV-SV40
DHFR
6.7 kb
BglII
M13
ori
SV40
ori
DHFR
x HindIII - XbaI
HindIII
PstI
SalI
ClaI
BamHI
KpnI
XhoI
EcoRI
XbaI
CMV
ori
splice
+ An
Amp
pAD-CMV1
6.4 kb
BglII
M13
ori
SV40
ori
DHFR
XbaI
EcoRI
XhoI
KpnI
BamHI
ClaI
SalI
PstI
HindIII
CMV
ori
splice
+ An
Amp
pAD-CMV2
6.4 kb
BglII
M13
ori
SV40
ori
DHFR

FIG. 6A

pAD-CMV1 : 6414 bp

TCGACATTGA TTATTGACTA GTTATTAATA GTAATCAATT ACGGGGTCAT TAGTTCATAG 60
CCCATATATG GAGTTCCGCG TTACATAACT TACGGTAAAT GGCCCGCCTG GCTGACCGCC 120
CAACGACCCC CGCCCATTGA CGTCAATAAT GACGTATGTT CCCATAGTAA CGCCAATAGG 180
GACTTTCCAT TGACGTCAAT GGGTGGAGTA TTTACGGTAA ACTGCCCACT TGGCAGTACA 240
TCAAGTGTAT CATATGCCAA GTACGCCCCC TATTGACGTC AATGACGGTA AATGGCCCGC 300
CTGGCATTAT GCCCAGTACA TGACCTTATG GGACTTTCCT ACTTGGCAGT ACATCTACGT 360
ATTAGTCATC GCTATTACCA TGGTGATGCG GTTTTGGCAG TACATCAATG GGCGTGGATA 420
GCGGTTTGAC TCACGGGGAT TTCCAAGTCT CCACCCCATT GACGTCAATG GGAGTTTGTT 480
TTGGCACCAA AATCAACGGG ACTTTCCAAA ATGTCGTAAC AACTCCGCCC CATTGACGCA 540
AATGGGCGGT AGGCGTGTAC GGTGGGAGGT CTATATAAGC AGAGCTCTCT GGCTAACTAG 600
AGAACCCACT GCTTAACTGG CTTATCGAAA TTAATACGAC TCACTATAGG GAGACCCAAG 660
CTTCTGCAGG TCGACATCGA TGGATCCGGT ACCTCGAGCG CGAATTCTCT AGAGGATCTT 720
TGTGAAGGAA CCTTACTTCT GTGGTGTGAC ATAATTGGAC AAACTACCTA CAGAGATTTA 780
AAGCTCTAAG GTAAATATAA AATTTTTAAG TGTATAATGT GTTAAACTAC TGATTCTAAT 840
TGTTTGTGTA TTTTAGATTC CAACCTATGG AACTGATGAA TGGGAGCAGT GGTGGAATGC 900
CTTTAATGAG GAAAACCTGT TTTGCTCAGA AGAAATGCCA TCTAGTGATG ATGAGGCTAC 960
TGCTGACTCT CAACATTCTA CTCCTCCAAA AAAGAAGAGA AAGGTAGAAG ACCCCAAGGA 1020
CTTTCCTTCA GAATTGCTAA GTTTTTTGAG TCATGCTGTG TTTAGTAATA GAACTCTTGC 1080
TTGCTTTGCT ATTTACACCA CAAAGGAAAA AGCTGCACTG CTATACAAGA AAATTATGGA 1140
AAAATATTTG ATGTATAGTG CCTTGACTAG AGATCATAAT CAGCCATACC ACATTTGTAG 1200
AGGTTTTACT TGCTTTAAAA AACCTCCCAC ACCTCCCCCT GAACCTGAAA CATAAAATGA 1260
ATGCAATTGT TGTTGTTAAC TTGTTTATTG CAGCTTATAA TGGTTACAAA TAAAGCAATA 1320
GCATCACAAA TTTCACAAAT AAAGCATTTT TTTCACTGCA TTCTAGTTGT GGTTTGTCCA 1380
AACTCATCAA TGTATCTTAT CATGTCTGGA TCAATTCTGA GAAACTAGCC TTAAAGACAG 1440

FIG. 6B

ACAGCTTTGT TCTAGTCAGC CAGGCAAGCA TATGTAAATA AAGTTCCTCA GGGAACTGAG 1500

GTTAAAAGAT GTATCCTGGA CCTGCCAGAC CTGGCCATTC ACGTAAACAG AAGATTCCGC 1560

CTCAAGTTCC GGTTAACAAC AGGAGGCAAC GAGATCTCAA ATCTATTACT TCTAATCGGG 1620

TAATTAAAAC CTTTCAACTA AAACACGGAC CCACGGATGT CACCCACTTT TCCTTCCCCG 1680

GCTCCGCCCT TCTCAGTACT CCCCACCATT AGGCTCGCTA CTCCACCTCC ACTTCCGGGC 1740

GCGACACCCA CGTGCCCTCT CCCACCCGAC GCTAACCCCG CCCCTGCCCG TCTGACCCCG 1800

CCCACCACCT GGCCCCGCCC CGTTGAGGAC AGAAGAAACC CCGGGCAGCC GCAGCCAAGG 1860

CGGACGGGTA GACGCTGGGG GCGCTGAGGA GTCGTCCTCT ACCTTCTCTG CTGGCTCGGT 1920

GGGGGACGCG GTGGATCTCA GGCTTCCGGA AGACTGGAAG AACCGGCTCA GAACCGCTTG 1980

TCTCCGCGGG GCTTGGGCGG CGGAAGAATG GCCGCTAGAC GCGGACTTGG TGCGAGGCAT 2040

CGCAGGATGC AGAAGAGCAA GCCCGCCGGG AGCGCGCGGC TGTACTACCC CGCGCCTGGA 2100

GCGGCCACGC CGGACTGGGC GGGGCCGGCC TGGTGGAGGC GGAGTCTGAC CTCGTGGAGG 2160

CGGGGCCTCT GATGTTCAAA TAGGATGCTA GGCTTGTTGA GGCGTGGCCT CCGATTCACA 2220

AGTGGGAAGC AGCGCCGGGC GACTGCAATT TCGCGCCAAA CTTGGGGGAA GCACAGCGTA 2280

CAGGCTGCCT AGGTGATCGC TGCTGCTGTC ATGGTTCGAC CGCTGAACTG CATCGTCGCC 2340

GTGTCCCAGA ATATGGGCAT CGGCAAGAAC GGAGACCTTC CCTGGCCAAT GCTCAGGTAC 2400

TGGCTGGATT GGGTTAGGGA AACCGAGGCG GTTCGCTGAA TCGGGTCGAG CACTTGGCGG 2460

AGACGCGCGG GCCAACTACT TAGGGACAGT CATGAGGGGT AGGCCCGCCG GCTGCTGCCC 2520

TTGCCCATGC CCGCGGTGAT CCCCATGCTG TGCCAGCCTT TGCCCAGAGG CGCTCTAGCT 2580

GGGAGCAAAG TCCGGTCACT GGGCAGCACC ACCCCCCGGA CTTGCATGGG TAGCCGCTGA 2640

GATGGAGCCT GAGCACACGT GACAGGGTCC CTGTTAACGC AGTGTTTCTC TAACTTTCAG 2700

GAACGAGTTC AAGTACTTCC AAAGAATGAC CACCACCTCC TCAGTGGAAG GTAAACAGAA 2760

CCTGGTGATT ATGGGCCGGA AAACCTGGTT CTCCATTCCT GAGAAGAATC GACCTTTAAA 2820

GGACAGAATT AATATAGTTC TCAGTAGAGA GCTCAAGGAA CCACCACAAG GAGCTCATTT 2880

TCTTGCCAAA AGTCTGGACC ATGCCTTAAA ACTTATTGAA CAACCAGAGT TAGCAGATAA 2940

AGTGGACATG GTTTGGATAG TTGGAGGCAG TTCCGTTTAC AAGGAAGCCA TGAATCAGCC 3000

FIG. 6C

AGGCCATCTC AGACTCTTTG TGACAAGGAT CATGCAGGAA TTTGAAAGTG ACACGTTCTT 3060
CCCAGAAATT GATTTGGAGA AATATAAACT TCTCCCAGAG TACCCAGGGG TCCTTTCTGA 3120
AGTCCAGGAG GAAAAAGGCA TCAAGTATAA ATTTGAAGTC TATGAGAAGA AAGGCTAACA 3180
GAAAGATACT TGCTGATTGA CTTCAAGTTC TACTGCTTTC CTCCTAAAAT TATGCATTTT 3240
TACAAGACCA TGGGACTTGT GTTGGCTTTA GATCCTGTGC ATCCTGGGCA ACTGTTGTAC 3300
TCTAAGCCAC TCCCCAAAGT CATGCCCCAG CCCCTGTATA ATTCTAAACA ATTAGAATTA 3360
TTTTCATTTT CATTAGTCTA ACCAGGTTAT ATTAAATATA CTTTAAGAAA CACCATTTGC 3420
CATAAAGTTC TCAATGCCCC TCCCATGCAG CCTCAAGTGG CTCCCCAGCA GATGCATAGG 3480
GTAGTGTGTG TACAAGAGAC CCCAAAGACA TAGAGCCCCT GAGAGCATGA GCTGATATGG 3540
GGGCTCATAG AGATAGGAGC TAGATGAATA AGTACAAAGG GCAGAAATGG GTTTTAACCA 3600
GCAGAGCTAG AACTCAGACT TTAAAGAAAA TTAGATCAAA GTAGAGACTG AATTATTCTG 3660
CACATCAGAC TCTGAGCAGA GTTCTGTTCA CTCAGACAGA AAATGGGTAA ATTGAGAGCT 3720
GGCTCCATTG TGCTCCTTAG AGATGGGAGC AGGTGGAGGA TTATATAAGG TCTGGAACAT 3780
TTAACTTCTC CGTTTCTCAT CTTCAGTGAG ATTCCAAGGG ATACTACAAT TCTGTGGAAT 3840
GTGTGTCAGT TAGGGTGTGG AAAGTCCCCA GGCTCCCCAG CAGGCAGAAG TATGCAAAGC 3900
ATGCATCTCA ATTAGTCAGC AACCAGGTGT GGAAAGTCCC CAGGCTCCCC AGCAGGCAGA 3960
AGTATGCAAA GCATGCATCT CAATTAGTCA GCAACCATAG TCCCGCCCCT AACTCCGCCC 4020
ATCCCGCCCC TAACTCCGCC CAGTTCCGCC CATTCTCCGC CCCATGGCTG ACTAATTTTT 4080
TTTATTTATG CAGAGGCCGA GGCGCCTCTG AGCTATTCCA GAAGTAGTGA GGAGGCTTTT 4140
TTGGAGGCCT AGGCTTTTGC AAAAAAGCTA ATTCAGCCTG AATGGCGAAT GGGACGCGCC 4200
CTGTAGCGGC GCATTAAGCG CGGCGGGTGT GGTGGTTACG CGCAGCGTGA CCGCTACACT 4260
TGCCAGCGCC CTAGCGCCCG CTCCTTTCGC TTTCTTCCCT TCCTTTCTCG CCACGTTCGC 4320
CGGCTTTCCC CGTCAAGCTC TAAATCGGGG GCTCCCTTTA GGGTTCCGAT TTAGTGCTTT 4380
ACGGCACCTC GACCCCAAAA ACTTGATTAG GGTGATGGTT CACGTAGTGG GCCATCGCCC 4440
TGATAGACGG TTTTTCGCCC TTTGACGTTG GAGTCCACGT TCTTTAATAG TGGACTCTTG 4500
TTCCAAACTG GAACAACACT CAACCCTATC TCGGTCTATT CTTTTGATTT ATAAGGGATT 4560

FIG. 6D

TTGCCGATTT CGGCCTATTG GTTAAAAAAT GAGCTGATTT AACAAAAATT TAACGCGAAT 4620

TTTAACAAAA TATTAACGTT TACAATTTCA GGTGGCACTT TTCGGGGAAA TGTGCGCGGA 4680

ACCCCTATTT GTTTATTTTT CTAAATACAT TCAAATATGT ATCCGCTCAT GAGACAATAA 4740

CCCTGATAAA TGCTTCAATA ATATTGAAAA AGGAAGAGTA TGAGTATTCA ACATTTCCGT 4800

GTCGCCCTTA TTCCCTTTTT TGCGGCATTT TGCCTTCCTG TTTTTGCTCA CCCAGAAACG 4860

CTGGTGAAAG TAAAAGATGC TGAAGATCAG TTGGGTGCAC GAGTGGGTTA CATCGAACTG 4920

GATCTCAACA GCGGTAAGAT CCTTGAGAGT TTTCGCCCCG AAGAACGTTT TCCAATGATG 4980

AGCACTTTTA AAGTTCTGCT ATGTGGCGCG GTATTATCCC GTATTGACGC CGGGCAAGAG 5040

CAACTCGGTC GCCGCATACA CTATTCTCAG AATGACTTGG TTGAGTACTC ACCAGTCACA 5100

GAAAAGCATC TTACGGATGG CATGACAGTA AGAGAATTAT GCAGTGCTGC CATAACCATG 5160

AGTGATAACA CTGCGGCCAA CTTACTTCTG ACAACGATCG GAGGACCGAA GGAGCTAACC 5220

GCTTTTTTGC ACAACATGGG GGATCATGTA ACTCGCCTTG ATCGTTGGGA ACCGGAGCTG 5280

AATGAAGCCA TACCAAACGA CGAGCGTGAC ACCACGATGC CTGTAGCAAT GGCAACAACG 5340

TTGCGCAAAC TATTAACTGG CGAACTACTT ACTCTAGCTT CCCGGCAACA ATTAATAGAC 5400

TGGATGGAGG CGGATAAAGT TGCAGGACCA CTTCTGCGCT CGGCCCTTCC GGCTGGCTGG 5460

TTTATTGCTG ATAAATCTGG AGCCGGTGAG CGTGGGTCTC GCGGTATCAT TGCAGCACTG 5520

GGGCCAGATG GTAAGCCCTC CCGTATCGTA GTTATCTACA CGACGGGGAG TCAGGCAACT 5580

ATGGATGAAC GAAATAGACA GATCGCTGAG ATAGGTGCCT CACTGATTAA GCATTGGTAA 5640

CTGTCAGACC AAGTTTACTC ATATATACTT TAGATTGATT TAAAACTTCA TTTTTAATTT 5700

AAAAGGATCT AGGTGAAGAT CCTTTTTGAT AATCTCATGA CCAAAATCCC TTAACGTGAG 5760

TTTTCGTTCC ACTGAGCGTC AGACCCCGTA GAAAAGATCA AAGGATCTTC TTGAGATCCT 5820

TTTTTTCTGC GCGTAATCTG CTGCTTGCAA ACAAAAAAAC CACCGCTACC AGCGGTGGTT 5880

TGTTTGCCGG ATCAAGAGCT ACCAACTCTT TTTCCGAAGG TAACTGGCTT CAGCAGAGCG 5940

CAGATACCAA ATACTGTCCT TCTAGTGTAG CCGTAGTTAG GCCACCACTT CAAGAACTCT 6000

GTAGCACCGC CTACATACCT CGCTCTGCTA ATCCTGTTAC CAGTGGCTGC TGCCAGTGGC 6060

GATAAGTCGT GTCTTACCGG GTTGGACTCA AGACGATAGT TACCGGATAA GGCGCAGCGG 6120

FIG. 6E

```
TCGGGCTGAA CGGGGGGTTC GTGCACACAG CCCAGCTTGG AGCGAACGAC CTACACCGAA   6180

CTGAGATACC TACAGCGTGA GCATTGAGAA AGCGCCACGC TTCCCGAAGG GAGAAAGGCG   6240

GACAGGTATC CGGTAAGCGG CAGGGTCGGA ACAGGAGAGC GCACGAGGGA GCTTCCAGGG   6300

GGAAACGCCT GGTATCTTTA TAGTCCTGTC GGGTTTCGCC ACCTCTGACT TGAGCGTCGA   6360

TTTTTGTGAT GCTCGTCAGG GGGGCGGAGC CTATGGAAAA ACGCCAGCAA CGCC
```

FIG. 7A

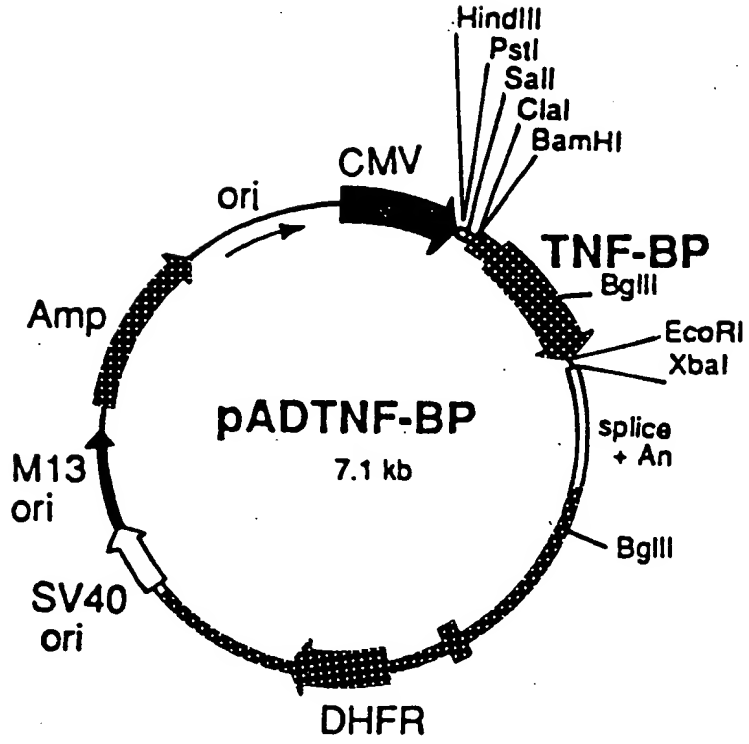


FIG. 7B

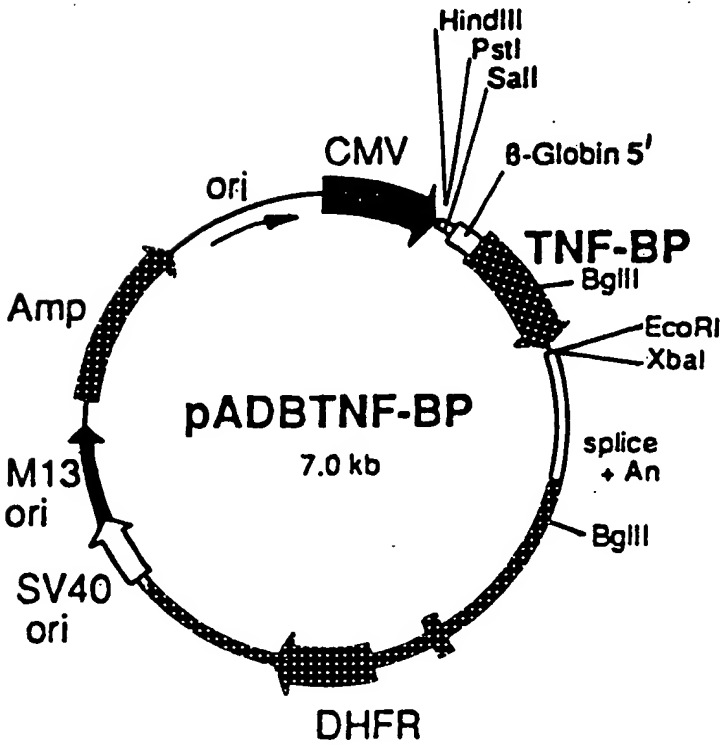


FIG. 7C

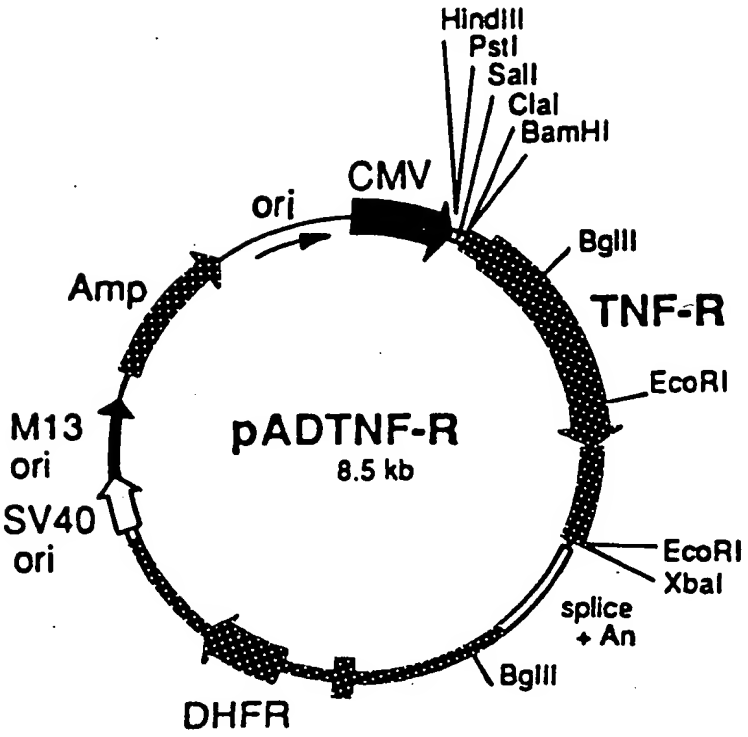

HindIII
PstI
SalI
ClaI
BamHI
CMV
ori
BglII
Amp
TNF-R
EcoRI
M13
ori
pADTNF-R
8.5 kb
SV40
ori
EcoRI
XbaI
splice
+ An
BglII
DHFR

FIG. 7D

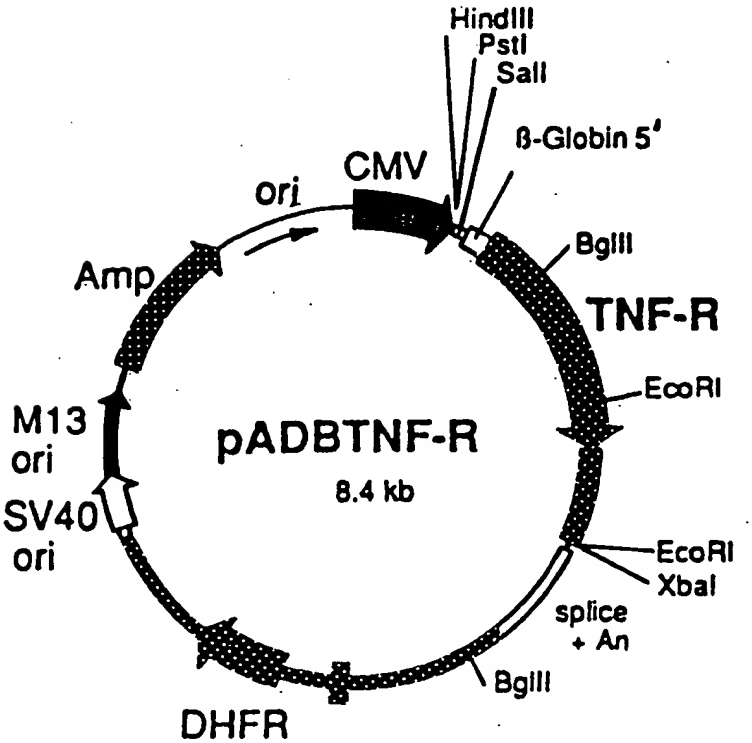

HindIII
PstI
SalI
ß-Globin 5'
CMV
ori
BglII
Amp
TNF-R
EcoRI
M13
ori
pADBTNF-R
8.4 kb
SV40
ori
EcoRI
XbaI
splice
+ An
BglII
DHFR

FIG. 8A

raTNF-R

```
GAATTCCTTT TCTCCGAGTT TTCTGAACTC TGGCTCATGA TCGGGCTTAC TGGATACGAG      60
AATCCTGGAG, GACCGTACCC TGATTTCCAT CTACCTCTGA CTTTGAGCCT TTCTAACCCG     120
GGGCTCACGC TGCCAACACC CGGGCCACCT GGTCCGATCG TCTTACTTCA TTCACCAGCG     180
TTGCCAATTG CTGCCCTGTC CCCAGCCCCA ATGGGGGAGT GAGAGAGGCC ACTGCCGGCC     240
GGAC
245/1                                          275/11
ATG GGT CTC CCC ATC GTG CCT GGC CTG CTG CTG TCA CTG GTG CTC CTG GCT CTG CTG ATG
Met Gly Leu Pro Ile Val Pro Gly Leu Leu Leu Ser Leu Val Leu Leu Ala Leu Leu Met
305/21                                         335/31
GGG ATA CAC CCA TCA GGG GTC ACC GGA CTG GTT CCT TCT CTT GGT GAC CGG GAG AAG AGG
Gly Ile His Pro Ser Gly Val Thr Gly Leu Val Pro Ser Leu Gly Asp Arg Glu Lys Arg
365/41                                         395/51
GAT AAT TTG TGT CCC CAG GGA AAG TAT GCC CAT CCA AAG AAT AAT TCC ATC TGC TGC ACC
Asp Asn Leu Cys Pro Gln Gly Lys Tyr Ala His Pro Lys Asn Asn Ser Ile Cys Cys Thr
425/61                                         455/71
AAG TGC CAC AAA GGA ACC TAC TTG GTG AGT GAC TGT CCA AGC CCA GGG CAG GAA ACA GTC
Lys Cys His Lys Gly Thr Tyr Leu Val Ser Asp Cys Pro Ser Pro Gly Gln Glu Thr Val
485/81                                         515/91
TGC GAG CTC TCT CAT AAA GGC ACC TTT ACA GCT TCG CAG AAC CAC GTC AGA CAG TGT CTC
Cys Glu Leu Ser His Lys Gly Thr Phe Thr Ala Ser Gln Asn His Val Arg Gln Cys Leu
545/101                                        575/111
AGT TGC AAG ACA TGT CGG AAA GAA ATG TTC CAG GTG GAG ATT TCT CCT TGC AAA GCT GAC
Ser Cys Lys Thr Cys Arg Lys Glu Met Phe Gln Val Glu Ile Ser Pro Cys Lys Ala Asp
605/121                                        635/131
ATG GAC ACC GTG TGT GGC TGC AAG AAG AAC CAA TTC CAG CGC TAC CTG AGT GAG ACG CAT
Met Asp Thr Val Cys Gly Cys Lys Lys Asn Gln Phe Gln Arg Tyr Leu Ser Glu Thr His
665/141                                        695/151
TTC CAG TGT GTG GAC TGC AGC CCC TGC TTC AAT GGC ACC GTG ACA ATC CCC TGT AAG GAG
Phe Gln Cys Val Asp Cys Ser Pro Cys Phe Asn Gly Thr Val Thr Ile Pro Cys Lys Glu
725/161                                        755/171
AAA CAG AAC ACC GTG TGT AAC TGC CAC GCA GGA TTC TTT CTA AGC GGA AAT GAG TGC ACC
Lys Gln Asn Thr Val Cys Asn Cys His Ala Gly Phe Phe Leu Ser Gly Asn Glu Cys Thr
785/181                                        815/191
CCT TGC AGC CAC TGC AAG AAA AAT CAG GAA TGT ATG AAG CTG TGC CTA CCT CCA GTT GCA
Pro Cys Ser His Cys Lys Lys Asn Gln Glu Cys Met Lys Leu Cys Leu Pro Pro Val Ala
845/201                                        875/211
AAT GTC ACA AAC CCC CAG GAC TCA GGT ACT GCC GTG CTG TTG CCT CTG GTT ATC TTC CTA
Asn Val Thr Asn Pro Gln Asp Ser Gly Thr Ala Val Leu Leu Pro Leu Val Ile Phe Leu
905/221                                        935/231
GGT CTT TGC CTT TTA TTC TTT ATC TGC ATC AGT CTA CTG TGC CGA TAT CCC CAG TGG AGG
Gly Leu Cys Leu Leu Phe Phe Ile Cys Ile Ser Leu Leu Cys Arg Tyr Pro Gln Trp Arg
965/241                                        995/251
CCC AGG GTC TAC TCC ATC ATT TGT AGG GAT TCA GCT CCT GTC AAA GAG GTG GAG GGT GAA
Pro Arg Val Tyr Ser Ile Ile Cys Arg Asp Ser Ala Pro Val Lys Glu Val Glu Gly Glu
1025/261                                       1055/271
GGA ATT GTT ACT AAG CCC CTA ACT CCA GCC TCT ATC CCA GCC TTC AGC CCC AAC CCC GGC
Gly Ile Val Thr Lys Pro Leu Thr Pro Ala Ser Ile Pro Ala Phe Ser Pro Asn Pro Gly
1085/281                                       1115/291
TTC AAC CCC ACT CTG GGC TTC AGC ACC ACC CCA CGC TTC AGT CAT CCT GTC TCC AGT ACC
Phe Asn Pro Thr Leu Gly Phe Ser Thr Thr Pro Arg Phe Ser His Pro Val Ser Ser Thr
1145/301                                       1175/311
CCC ATC AGC CCC GTC TTC GGT CCT AGT AAC TGG CAC AAC TTC GTG CCA CCT GTA AGA GAG
Pro Ile Ser Pro Val Phe Gly Pro Ser Asn Trp His Asn Phe Val Pro Pro Val Arg Glu
1205/321                                       1235/331
GTG GTC CCA ACC CAG GGT GCT GAC CCT CTC CTC TAC GGA TCC CTC AAC CCT GTG CCA ATC
Val Val Pro Thr Gln Gly Ala Asp Pro Leu Leu Tyr Gly Ser Leu Asn Pro Val Pro Ile
```

FIG. 8B

```
1265/341                                   1295/351
CCC GCC CCT GTT CGG AAA TGG GAA GAC GTC GTC GCG GCC CAG CCA CAA CGG CTT GAC ACT
Pro Ala Pro Val Arg Lys Trp Glu Asp Val Val Ala Ala Gln Pro Gln Arg Leu Asp Thr
1325/361                                   1355/371
GCA GAC CCT GCG ATG CTG TAT GCT GTG GTG GAT GGC GTG CCT CCG ACA CGC TGG AAG GAG
Ala Asp Pro Ala Met Leu Tyr Ala Val Val Asp Gly Val Pro Pro Thr Arg Trp Lys Glu
1385/381                                   1415/391
TTC ATG CGG CTC CTG GGG CTG AGC GAG CAC GAG ATC GAG CGG CTG GAG CTG CAG AAC GGG
Phe Met Arg Leu Leu Gly Leu Ser Glu His Glu Ile Glu Arg Leu Glu Leu Gln Asn Gly
1445/401                                   1475/411
CGT TGC CTC CGC GAG GCT CAT TAC AGC ATG CTG GAA GCC TGG CGG CGC CGC ACA CCG CGA
Arg Cys Leu Arg Glu Ala His Tyr Ser Met Leu Glu Ala Trp Arg Arg Arg Thr Pro Arg
1505/421                                   1535/431
CAC GAG GCC ACG CTG GAC GTA GTG GGC CGC GTG CTT TGC GAC ATG AAC CTG CGT GGC TGC
His Glu Ala Thr Leu Asp Val Val Gly Arg Val Leu Cys Asp Met Asn Leu Arg Gly Cys
1565/441                                   1595/451
CTG GAG AAC ATC CGC GAG ACT CTA GAA AGC CCT GCC CAC TCG TCC ACG ACC CAC CTC CCG
Leu Glu Asn Ile Arg Glu Thr Leu Glu Ser Pro Ala His Ser Ser Thr Thr His Leu Pro
1625/461
CGA TAA
Arg Stop
           GGCCACACCC CCACCTCAGG AACGGGACTC GAAGGACCAT CCTGCTAGAT   1680
GCCCTGCTTC CCTGTGAACC TCCTCTTTGG TCCTCTAGGG GGCAGGCTCG ATCTGGCAGG   1740
CTCGATCTGG CAGCCACTTC CTTGGTGCTA CCGACTTGGT GTACATAGCT TTTCCCAGCT   1800
GCCGAGGACA GCCTGTGCCA GCCACTTGTG CATGGCAGGG AAGTGTGCCA TCTGCTCCCA   1860
GACAGCTGAG GGTGCCAAAA GCCAGGAGAG GTGATTGTGG AGAAAAAGCA CAATCTATCT   1920
GATACCCACT TGGGATGCAA GGACCCAAAC AAAGCTTCTC AGGGCCTCCT CAGTTGATTT   1980
CTGGGCCCTT TTCACAGTAG ATAAAACAGT CTTTGTATTG ATTATATCAC ACTAATGGAT   2040
GAACGGTTGA ACTCCCTAAG GTAGGGGCAA GCACAGAACA GTGGGGTCTC CAGCTGGAGC   2100
CCCCGACTCT TGTAAATACA CTAAAAATCT AAAAGTGAAA AAAAAAAAAA AAAAAAAAAA   2160
AAAAAAGGAA TTC
```

FIG. 9A

huTNF-R

```
GAATTCTCTG GACTGAGGCT CCAGTTCTGG CCTTTGGGGT TCAAGATCAC TGGGACCAGG      60
CCGTGATCTC TATGCCCGAG TCTCAACCCT CAACTGTCAC CCCAAGGCAC TTGGGACGTC     120
CTGGACAGAC CGAGTCCCGG GAAGCCCCAG CACTGCCGCT GCCACACTGC CCTGAGCCCA     180
AATGGGGGAG TGAGAGGCCA TAGCTGTCTG GC

213/1                                           243/11
ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG
Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val
273/21                                          303/31
GGA ATA TAC CCC TCA GGG GTT ATT GGA CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA
Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg
333/41                                          363/51
GAT AGT GTG TGT CCC CAA GGA AAA TAT ATC CAC CCT CAA AAT AAT TCG ATT TGC TGT ACC
Asp Ser Val Cys Pro Gln Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr
393/61                                          423/71
AAG TGC CAC AAA GGA ACC TAC TTG TAC AAT GAC TGT CCA GGC CCG GGG CAG GAT ACG GAC
Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp
453/81                                          483/91
TGC AGG GAG TGT GAG AGC GGC TCC TTC ACC GCT TCA GAA AAC CAC CTC AGA CAC TGC CTC
Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu
513/101                                         543/111
AGC TGC TCC AAA TGC CGA AAG GAA ATG GGT CAG GTG GAG ATC TCT TCT TGC ACA GTG GAC
Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val Glu Ile Ser Ser Cys Thr Val Asp
573/121                                         603/131
CGG GAC ACC GTG TGT GGC TGC AGG AAG AAC CAG TAC CGG CAT TAT TGG AGT GAA AAC CTT
Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu
633/141                                         663/151
TTC CAG TGC TTC AAT TGC AGC CTC TGC CTC AAT GGG ACC GTG CAC CTC TCC TGC CAG GAG
Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu
693/161                                         723/171
AAA CAG AAC ACC GTG TGC ACC TGC CAT GCA GGT TTC TTT CTA AGA GAA AAC GAG TGT GTC
Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu Asn Glu Cys Val
753/181                                         783/191
TCC TGT AGT AAC TGT AAG AAA AGC CTG GAG TGC ACG AAG TTG TGC CTA CCC CAG ATT GAG
Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr Lys Leu Cys Leu Pro Gln Ile Glu
813/201                                         843/211
AAT GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA GTG CTG TTG CCC CTG GTC ATT TTC TTT
Asn Val Lys Gly Thr Glu Asp Ser Gly Thr Thr Val Leu Leu Pro Leu Val Ile Phe Phe
873/221                                         903/231
GGT CTT TGC CTT TTA TCC CTC CTC TTC ATT GGT TTA ATG TAT CGC TAC CAA CGG TGG AAG
Gly Leu Cys Leu Leu Ser Leu Leu Phe Ile Gly Leu Met Tyr Arg Tyr Gln Arg Trp Lys
933/241                                         963/251
TCC AAG CTC TAC TCC ATT GTT TGT GGG AAA TCG ACA CCT GAA AAA GAG GGG GAG CTT GAA
Ser Lys Leu Tyr Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys Glu Gly Glu Leu Glu
993/261                                         1023/271
GGA ACT ACT ACT AAG CCC CTG GCC CCA AAC CCA AGC TTC AGT CCC ACT CCA GGC TTC ACC
Gly Thr Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser Phe Ser Pro Thr Pro Gly Phe Thr
1053/281                                        1083/291
CCC ACC CTG GGC TTC AGT CCC GTG CCC AGT TCC ACC TTC ACC TCC AGC TCC ACC TAT ACC
Pro Thr Leu Gly Phe Ser Pro Val Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr Tyr Thr
1113/301                                        1143/311
CCC GGT GAC TGT CCC AAC TTT GCG GCT CCC CGC AGA GAG GTG GCA CCA CCC TAT CAG GGG
Pro Gly Asp Cys Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro Pro Tyr Gln Gly
1173/321                                        1203/331
GCT GAC CCC ATC CTT GCG ACA GCC CTC GCC TCC GAC CCC ATC CCC AAC CCC CTT CAG AAG
Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp Pro Ile Pro Asn Pro Leu Gln Lys
```

FIG. 9B

```
1233/341                                            1263/351
TGG GAG GAC AGC GCC CAC AAG CCA CAG AGC CTA GAC ACT GAT GAC CCC GCG ACG CTG TAC
Trp Glu Asp Ser Ala His Lys Pro Gln Ser Leu Asp Thr Asp Asp Pro Ala Thr Leu Tyr
1293/361                                            1323/371
GCC GTG GTG GAG AAC GTG CCC CCG TTG CGC TGG AAG GAA TTC GTG CGG CGC CTA GGG CTG
Ala Val Val Glu Asn Val Pro Pro Leu Arg Trp Lys Glu Phe Val Arg Arg Leu Gly Leu
1353/381                                            1383/391
AGC GAC CAC GAG ATC GAT CGG CTG GAG CTG CAG AAC GGG CGC TGC CTG CGC GAG GCG CAA
Ser Asp His Glu Ile Asp Arg Leu Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln
1413/401                                            1443/411
TAC AGC ATG CTG GCG ACC TGG AGG CGG CGC ACG CCG CGG CGC GAG GCC ACG CTG GAG CTG
Tyr Ser Met Leu Ala Thr Trp Arg Arg Arg Thr Pro Arg Arg Glu Ala Thr Leu Glu Leu
1473/421                                            1503/431
CTG GGA CGC GTG CTC CGC GAC ATG GAC CTG CTG GGC TGC CTG GAG GAC ATC GAG GAG GCG
Leu Gly Arg Val Leu Arg Asp Met Asp Leu Leu Gly Cys Leu Glu Asp Ile Glu Glu Ala
1533/441                                            1563/451
CTT TGC GGC CCC GCC GCC CTC CCG CCC GCG CCC AGT CTT CTC AGA TGA              1580
Leu Cys Gly Pro Ala Ala Leu Pro Pro Ala Pro Ser Leu Leu Arg Stop

GGCTGCGCCC CTGCGGGCAG CTCTAAGGAC CGTCCTGCGA   1620
GATCGCCTTC CAACCCCACT TTTTTCTGGA AAGGAGGGGT CCTGCAGGGG CAAGCAGGAG   1680
CTAGCAGCCG CCTACTTGGT GCTAACCCCT CGATGTACAT AGCTTTTCTC AGCTGCCTGC   1740
GCGCCGCCGA CAGTCAGCGC TGTGCGCGCG GAGAGAGGTG CGCCGTGGGC TCAAGAGCCT   1800
GAGTGGGTGG TTTGCGAGGA TGAGGGACGC TATGCCTCAT GCCCGTTTTG GGTGTCCTCA   1860
CCAGCAAGGC TGCTCGGGGG CCCCTGGTTC GTCCCTGAGC CTTTTTCACA GTGCATAAGC   1920
AGTTTTTTTT GTTTTTGTTT TGTTTTGTTT TGTTTTTAAA TCAATCATGT TACACTAATA   1980
GAAACTTGGC ACTCCTGTGC CCTCTGCCTG GACAAGCACA TAGCAAGCTG AACTGTCCTA   2040
AGGCAGGGGC GAGCACGGAA CAATGGGGCC TTCAGCTGGA GCTGTGGACT TTTGTACATA   2100
CACTAAAATT CTGAAGTTAA AAAAAAAAAA AAAAGGAATT C                        2141
```

FIG.10